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A REVIEW OF MEIBOMIAN GLAND DYSFUNCTION AS PRESENTED AT DRY EYE UNIVERSITY

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Meibomian gland dysfunction (MGD), has been well established as a major etiologic factor in dry eye disease, replacing long regarded aqueous deficiency. Lemp, et al reported that 86% of a dry eye clinic cohort demonstrated evidence of MGD.[1] An understanding of normal meibomian gland function is important to effective dry eye management.

The meibomian glands within the tarsal plate are apocrine glands which release meibum secretions into the tear film from orifices in the posterior eyelid margin. The complex polar and nonpolar lipids of the meibum form the outer lipid layer of the precorneal tear film. The outer lipid layer interrelates with the underlying mucoaqueous protein layer which adheres to the epithelium of the outer surface.[2] It also protects the tear film from evaporation loss to the air when the eye is exposed between blinks. The outer lid layer thus contributes to tear film stability. Normal meibomian gland function is therefore requisite for optimal ocular surface health and homeostasis.

MGD has been defined as a diffuse disorder of the meibomian glands characterized by terminal duct obstruction and/or quantitative or qualitative alteration of the meibum secretions.[3] The consequence of meibomian gland obstruction and meibum alterations is a functional reduction in the thickness of the lipid layer of the tear film. This results is tear film hyperosmolarity, tear film instability, ocular surface inflammation, and ocular surface injury. These sequelae of MGD represent the etiologic factors described in the current Dry Eye Workshop consensus definition of dry eye disease. MGD is further characterized as a chronic progressive disorder that results in structural alterations and eventual atrophy of the meibomian glands which is irreparable. The understanding of MGD from the perspective of altered gland function and structure provides a framework for diagnosis and management similar to the established approach to glaucoma which all eye care providers are familiar with. In glaucoma, the clinical approach relies on structural metrics of optic disc appearance and peripapillary retinal nerve fiber thickness to detect and monitor progression. These metrics are further useful in establishing the effectiveness of therapeutic intervention.

MGD may be readily detected clinically by the appearance of the lid margin which includes pouting gland orifices, gland inspissation, tylosis, telangiectasia, and lid margin notching. Eyelid puffiness, erythema, and tenderness may also be present. Thickened meibum secretions may be expressed with compression of the lid. These findings represent obvious MGD. These are advanced MGD manifestations resulting from inflammatory lid margin and gland damage.

The more prevalent form of MGD is not associated with inflammatory lid margin alterations and is referred to as nonobvious MGD. The lid margin may look healthy, but gland expression may yield thick wax-like meibum or no secretions at all. Nonobvious MGD may be easily overlooked with no clinical findings evident. As MGD is felt to be progressive, obvious MGD most likely begins as nonobvious MGD, then becomes clinically apparent as inflammatory lid margin damage ensues. Because chronic disease management is more favourable with early intervention,

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MGD like glaucoma, must rely on clinical metrics of meibomian gland structures and function for optimal diagnosis and management.

Abnormal metrics indicating altered meibomian gland function or structural damage may establish medical necessity for therapeutic intervention to address meibomian gland obstruction. Early intervention is warranted to halt or avoid structural damage, as well as, prevent further compromise of gland function. This approach to meibomian gland disease represents a paradigm shift in the management of dry eye disease. In the past, dry eye disease was approached based on symptomatic awareness resulting from the sequela of inflammatory changes to the ocular surface. The current approach to dry eye disease is proactive, measurable, and more effective as it is directed to the root cause of MGD, which is present in the majority of cases. MGD is detected by screening using validated metrics, then treated in a fashion to relieve meibomian gland obstruction and promote healthy gland function.

METRICS IN MGD

Clinically validated metrics of meibomian gland structure include baseline and serial meibography. Meibographic images of MGD include gland widening, truncation, and drop out indicative of progressive gland atrophy. The meibomian glands may be clinically visualized by transillumination with a muscle light, however subtle alterations may be overlooked. High-resolution meibography imaging permits early-stage detection and serial monitor of gland structural changes over time with greater precision and reproducibility.

Clinically validated metrics of gland function include counting the number of functional meibomian glands and the number of expressible meibomian glands. Also, clinical grading of the expressed meibum appearance and interferometry measure the tear film lipid layer thickness provide useful metrics of gland function. The determination of functional glands involves lower lid compression with the Korb meibomian gland evaluator. Fifteen glands are challenged with compression over the lateral middle, and medial tarsal plate with the Korb MGE. The Korb MGE provides a controlled compression of 1 gram/cm^2 which approximates the pressure exerted on the meibomian gland during a deliberate blink.[4] The functional meibomian gland is one that yields liquid meibum secretions with a deliberate blink. Korb and Blackie demonstrated with statistical significance an inverse correlation between the number of lower lid functional glands and the severity of dry eye symptoms. They established that less than 6 functional glands correlated with the presence of dry eye disease.

The meibomian gland score represents the product of the number of functional lower lid glands among 15 glands challenged with the Korb MGE and the clinical meibum grade (0 to 3). The MG score provides us reproducible and validated metrics in gland function.

The expressible meibomian gland count in the lower lid is established by firm tarsal compression with a Q-tip against the globe. Expressible glands are deemed partially obstructed and distinguished from totally obstructed glands. This distinction has bearing on therapeutic options discussed later.

The tear film lipid layer thickness may be measured by quantitative interferometry. The healthy tear film has a lipid layer thickness is over 100 nanometers. The reduced lipid layer thickness is indicative of meibomian gland obstruction or meibum alteration. Qualitative interferometry may permit a less precise method of assessing meibomian gland function. Any measured compromise of meibomian gland function presents an indication for therapeutic intervention.

MGD TREATMENT

The management of MGD is directed toward the restoration of meibomian gland function and halting the progression of gland atrophy. Core therapy refers to the removal of distal gland ductal obstruction with the improved release of meibum secretions. Supplemental therapy refers to measures designed to reduce ocular surface inflammation, maintain gland orifice patency, and improve meibum secretion quality.

Patient education regarding lifestyle risk factors for MGD is an important component of supplemental therapy, as well. Increased disease awareness by the patient contributes to improved compliance with supplemental measures. It also enhances patient receptiveness to therapeutic procedures proposed initially and in the future. Patients must be educated regarding the unfamiliar proactive approach to MGD

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management in dry eye disease. They have preconceived notions regarding dry eye management based on previous encounters with eye care providers.

It is of value to establish a protocol for office visit frequency and diagnostic testing frequency to guide the interval between therapeutic interventions along with the selection of different options. The MGD metrics may establish that the patient may be responding to initial intervention or that no clinical effect has been realized. Modification of the treatment protocol may be guided by validated MGD metrics, and to a lesser extent, clinical symptoms.

Currently available core therapy procedures include automated and manual thermal pulsation. Automated thermopulsation with LipiFlow (J&J) has been available since 2012 and has a significant body of clinical research support in its therapeutic efficacy. Manual thermopulsation is available in 2 devices, the iLux (Alcon) and Tear Care (Sight Sciences). These newer options have been FDA approved since 2018. Thermopulsation devices provide temperature-controlled heat delivery to the lid margin and tarsus with controlled eyelid compression with the expression of the liquefied meibum secretions. The LipiFlow and iLux devices deliver heat to the posterior aspect of each eyelid before compression. The Tear Care treatment relies on customized anterior lid skin heat delivery. In my clinical experience, the duration of benefit with LipiFlow ranges from one to 3 years but varies with the number of expressible glands, the patient diligence of the patient with supplemental measures, and the extent of gland atrophy. The iLux and Tear Care treatment-duration of benefit has been 6 to 8 months in the author's practice. These manual interventions are utilized at 6 to 8-month intervals following LipiFlow to prolong its duration of benefit.

Meibomian gland probing with gland expression has been particularly effective to address total gland obstruction as a standalone procedure and in conjunction with thermal pulsation therapy. The distal gland intraductal obstruction may be breached with the 2 mm wire probe at the slit lamp following local infiltration of 2% Lidocaine or topical 8% Lidocaine in Jojoba wax application. Subsequent lid compression reveals the appearance of the inspissated meibum secretions as well as the relative volume of material. Slit lamp camera capability provides a compelling visual validation of the therapeutic approach. A review of the meibography may be helpful to set MG probing expectations as well.

Meibomian gland probing is particularly indicated when the number of expressible glands in the lid is significantly less than the number of glands anatomically present in meibography images. MG probing may improve the efficacy of thermal pulsation therapy by increasing the number of patent gland orifices yielding liquefied secretions. The usual therapeutic benefit of MG probing in the author's experience is around 6 to 9 months before a repeat intervention is warranted. However, with 6-8-month thermal pulsation and supplemental therapy, the decline in expressible gland count may be prolonged 1–3 years.

Supplemental measures are a number of maintenance lid care and adjunctive measures designed to reduce ocular surface inflammation, stabilize the tear film, and maintain meibomian gland function. These measures include lid scrub and thermal compresses administered by the patient at home regularly. Lipid stabilizing lubricants are used to support the tear film. Systemic macrolide and tetracycline derivative antibiotics in low doses with anti-inflammatory benefits to the eyelid. Topical aminoglycoside and macrolide antibiotics may be useful when a component of staphylococcal anterior blepharitis is present. Topical immunomodulation therapy of the ocular surface may include cyclosporine and lifitegrast in the long term and topical steroids for short term use. Ocular surface inflammation may also be reduced with oral omega -3 supplementation. oral omega -3 and precursor products may also improve meibum quality. Supplemental therapy office procedures include microblepharoexfoliation (BlephEx) and Intense Pulsed Light (IPL) therapy. Microblepharoexfoliation involves a microsponge cleaning of the lid margin and lashes. The lid scrub-soaked sponge tip is mounted on the spinning head of a handheld device. The BlephEx device provides effective removal of lid margin biofilm, bacteria, Demodex, and toxins which promote ocular surface inflammation.

IPL therapy is filtered visible light which is applied to the midfacial skin of fair-complexioned patients with rosacea to affect a reduction of lid erythema,

telangiectasia, and ocular surface inflammation. It is also thought to kill demodex which is felt to have an etiologic role in rosacea and demodex blepharitis which contribute to eyelid inflammation.[5] The True Tear device relies on neurostimulation of the afferent sensory nerves in the nasal walls to activate brainstem pathways which result in secretory regulation of the lacrimal functional unit, which includes the meibomian glands. The result of regular use of this modality is increased tear volume. The True Tear device provides adjunctive lubrication when eye drop frequency is inadequate due to work or lifestyle. These supplemental measures collectively maintain meibomian gland function once gland obstructions has been relieved.

When the treatment of the MGD appears to fail with persistent dry eye disease symptoms, several comorbidities must be considered. The most common factor is a component of exposure due to partial blink, lid deformity, lid retraction, and nocturnal lagophthalmos. Extensive meibomian gland atrophy in advanced MGD may significantly reduce the response to thermal pulsation and MG probing in addition to reducing the duration of the benefit. Cicatricial conjunctivitis, allergic conjunctivitis, and inflammatory blepharitis may also result in obliteration of meibomian gland orifices with subsequent gland atrophy. Systemic autoimmune disease states, particularly Sjogren's and Rheumatoid arthritis, may contribute to intractable ocular surface inflammation and injury further compromising meibomian gland function.

Meibomian gland disease management is an integral component in dry eye disease diagnosis and management. It provides a targeted, proactive, measurable, and effective approach to the most common etiologic component of dry eye disease. An understanding of meibomian gland function further facilitates the patient discussion regarding the impact of lifestyle and work-related visual demands which contribute to evaporative stress and ocular surface inflammation.

REFERENCES

1. Lemp MA, et al. Distribution of aqueous deficient and evaporative dry eye in a clinic- based patient cohort: A retrospective study. Corneal 2012;31(5):472–78.
2. Wilcox MDA, et al. TFOS DEWS II – Tear Film Report – Ocular Surf 2017;(3):366–403.
3. Geerling G, Tauber J, Baudain C, et al. The International Workshop on Meibomian Gland Dysfunction: report of the subcommittee on management and treatment of meibomian gland dysfunction. Invest Ophthalmol Vis Sci 2011; 52(4):2050–64.
4. Korb DR, Blackie CA. Meibomian gland diagnostic expressibility: correlation with dry eye symptoms and gland location. Corneal 2008;27 (10):1142–47.
5. Eitas R, et al. The rapid effect of pulsed eye laser on demodex density of facial skin. J Cosmet Laser Ther 2019;21(3):123–26.